Oral Diseases (2005) 11, 116–118

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LETTERS TO THE EDITOR

Letters to the Editor from Axéll, Zatterstrom, and Warnakulasuriya

The Editors are pleased to publish these three letters as a contribution to the debate on the important issue of carcinogenicity of oral smokeless tobaccos. In so doing it is prudent to bear in mind that the composition of such products, and the manner and intensity of their use, varies widely around the world. We must beware of generalizations.

Newell W Johnson
London
January 2005

Dear Sir(s)
I would like to comment on two articles in *Oral Diseases* published in the January issue 2004 and also to get a comment by the editor. The articles are written by Zatterstrom *et al* (2004) (Article A) and, as an Editorial, by Warnakulasuriya (2004) (Article B). The issue concerns the possible risk for developing cancer in Sweden after use of snuff and the possible causative role of snuff in this context, a heavily debated issue during the last decades. I will not include any political aspects on this matter when commenting on articles A and B but just comment on the scientific qualities. I have considered *Oral Diseases* as a journal for scientific articles and not for use for political ambitions. In order to specify this 'dilemma' I would like the editor(s) to answer or comment on my question below.

In the article by Zatterstrom *et al* (2004), one case of oral cancer is described. A 90-year-old man developed a cancer on 'the typical site … where he had allegedly placed the snuff since he was 20-year-old'. The authors further state that 'there seems to be little doubt that the cancer was associated with the patient's snuff taking', implying a causal association.

In the editorial by Warnakulasuriya, the author to some extent questions the results of two Swedish case control studies showing a lack of association between snuff (snus) use and oral cancer/cancer of the upper aerodigestive tract. Among else, the author refers to the fact that 'the Scandinavian studies do not have sufficient power to detect moderately raised OR'. In the same article the author refers to article A by Zatterstrom et al (2003) (wrong year!), without making any remark of its remarkable scientific weakness concerning showing a *causal* relationship between the use of snus and the development of cancer.

My question: *Does article A show a scientifically convincing causal relationship?* It should be emphasized that oral malignancies and potentially malignant lesions may very well appear in sites where individuals have allegedly placed snus. Three such cases of oral cancer were given account for in a retrospective Swedish study (Axéll *et al*, 1978). Figure 1 shows a proliferative verrucous leukoplakia (PVL) in a patient who has never used any kind of tobacco. According to a recent article by Bagan *et al* (2004), PVL develop oral squamous cell carcinoma in a very high frequency. Further, the patient described in article A also had removable dentures – could they theoretically 'cause' the cancer described?

Which out of articles A and B has the best design to elucidate the relationship between snuff (snus) use and oral cancer, or frankly, an acceptable design to be published? To me, article A has only shown that oral cancer may appear in individuals using snuff or wearing dentures. What is the *scientific* value of that? I can very well understand the *political* ambition of publishing article A – remarkably without any comment of its most limited scientific value in the Editorial article B, where the results of two case–control studies are questioned because of insufficient power – but I do not understand its place in a journal with an ambition to publish scientific material.

I would like to emphasize that a causal relationship between use of snus and the risk for developing oral cancer can never be solved in epidemiological case control studies or retrospective studies. As pointed out in article B, prospective studies of snus induced lesions are warranted to determine the risk for malignant change – if any. Such a study has recently been accounted for by Roosaar *et al* (2002). This type of

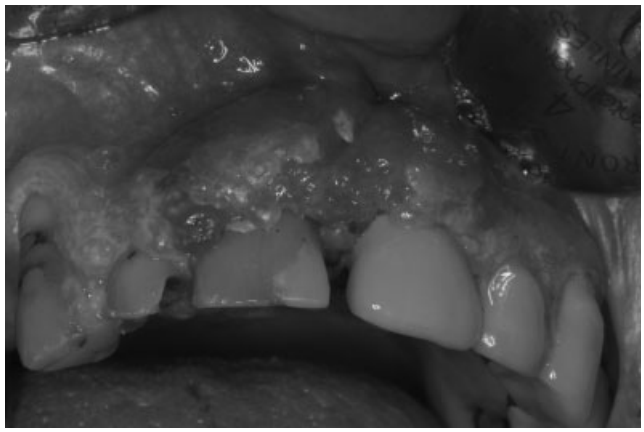

Figure 1 A 72-year-old man with a tumour in the maxillary front region. X-ray shows destruction of alveolar bone. The patient has never smoked or used tobacco in any other form. Preliminary histologic diagnosis: proliferative verrucous leukoplakia.

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study is though probably hampered by a low incidence of oral cancer and thereby by the need for following a substantial number of snus users for many years to attain a sufficiently high statistical power.

In conclusion: What is the scientific value of article A? Why publish the Editorial article B (with several other 'weaknesses' than the one we have focused on) with its uncritical mentioning of article A and on the same time depreciation of Swedish case–control studies?

Finally: Of course, the editorial staff of *Oral Diseases* has the right to make the journal a forum for political debate accepting any articles irrespective of their scientific value or quality – but then, this should be better defined and expressed in the scope of the journal.

Declaration of interest: Professor Axéll was a consultant to the Swedish Tobacco Company and a member of their Medical Research Council in the 1980s.

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Author A reply

Over the last decades in Sweden there has been a marked decline in smoking habits. Less than 20% of the population are now regular smokers. Many ex-smokers keep their longing for nicotine at bay by switching to the commonly used moist oral snuff that has long traditions in this country. The important question is whether this form of tobacco product is so harmless that health professionals even could recommend it as a safe way to quit smoking.

When moist snuff is used on a daily basis it induces local changes in the oral mucosa and the concern is that these focal lesions may over time transform into cancers. Although large epidemiological studies failed to correlate the use of Swedish snus (snuff) and the incidence of cancer in our country [*Cancer* 1998; **82**(7): 1367–1375, *Int J Cancer* 1998; **77**(3): 341–346], this does not rule out the risk for cancer in individual cases.

Our report describes a case where many years of snuff taking appeared to have caused a small cancer in the gingiva at the precise spot under the upper lip where Swedish snus had been placed for 70 years. We find it relevant to speculate that this may represent a snuff-induced lesion that had undergone malignant transformation. With the case report we want to draw attention to the fact that although using snuff is not as bad as smoking cigarettes, it is not totally harmless.

Declaration of interest: No conflicts asserted.

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